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Validation of Anti-GAGA4 IgM Antibodies for Predicting the Development of Relapsing Remitting Multiple Sclerosis after the First Neurological Event.

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Background: There is an unmet need to develop specific serum based biomarkers for the diagnosis and prognosis of Relapsing Remitting MS (RRMS). We have reported that elevated levels of serum anti-Glc(alpha1,4)Glc(alpha) (GAGA4) IgM antibodies (Ab) exist in RRMS (n=44) patients in comparison to patients with other neurological diseases (OND, n=44) enabling to discern which post-CIS patients convert to RRMS vs. OND. To validate our findings we have further investigate an additional and larger cohort of patients. ***Aim:*** To validate the predictive value of IgM Ab against GAGA4, for identifying of post CIS patients that will evolve to RRMS in a larger cohort. ***Methods:*** Retrospective analysis of 121 frozen sera taken from patients presenting for diagnostic work-up after a first acute neurological event consistent with demyelination (CIS) and were followed for a minimum of 4 years to confirm RRMS diagnosis. The "other neurological disease" (OND) control group comprised of 85 patients, 32 with other inflammatory disorders (OIND), and 53 with non-inflammatory neurological disease (ONIND). Sera were diluted 1:1200 and levels of anti GAGA4 IgM Ab measured by immunoassay normalized by dividing to square root of IgM levels (mg IgM/ml serum). ***Results:*** Significantly higher levels of anti-GAGA4 IgM/Total IgM (p=0.04, T test) Ab were observed in CIS patients who converted to RRMS as opposed to OND. Using a cut-off of 42 (anti GAGA4 IgM EU/(mg IgM /ml serum)$^{0.5}$), we have found that 34/121 (28%) converting CIS patients were positive, whereas 77/85 (91%) OND patients were negative, corresponding to a sensitivity of 28% (CI 95% 20.6-34.3%), a specificity of 91% (CI 95% 82.3-95.8%), PPV of 86.5%, and NPV of 36.4%. ***Conclusion:*** A higher level of Anti-GAGA4 IgM Ab was further validated as a predictor for the development of RRMS in CIS patients.

Key words: anti-glycan; antibody; biomarker, prediction